C-Reactive Protein (CRP): The Differences Amongst Various Assays

It has been brought to the Food and Drug Administration's attention that there may be confusion in the laboratory community, from clinicians and from manufacturers on the indications for use of different C-Reactive Protein (CRP) assays. This communication is intended to provide information about the differences of conventional CRP, high sensitivity CRP (hsCRP) and cardiac CRP (cCRP) assays and the regulatory need to designate a CRP assay specifically for cardiovascular risk indications for use. Much of this information is provided in *Guidance for Industry and FDA Staff - Review Criteria for Assessment of C Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays* which can be found at the following website: http://www.fda.gov/cdrh/oivd/guidance/1246.html.

In brief, the difference between hsCRP and cCRP is not in the analyte itself, but in the analytical performance which has been documented through submitted evidence. FDA is responsible for approving the device labeling (including the specifications stated in the package insert). When the device specifications indicate that the device can be used for multiple clinical purposes (e.g., to diagnose two distinct conditions or diseases), FDA requires appropriate evidence to support each clinical purpose. When, as in the case of CRP which is submitted with evidence of efficacy for cardiovascular risk stratification, FDA could have chosen to approve "High Sensitivity CRP-with-evidence-of-efficacy-for-identification-and-assessment/stratification-of-individuals-at-risk-for-future-cardiovascular-disease," but it chose instead to use the shorthand "Cardiac CRP (cCRP)"to distinguish such assays from "High Sensitivity CRP (hsCRP)" for which there is no evidence of efficacy in cardiovascular risk assessment/stratification. No hsCRP assay has been allowed to have this indication (cCRP) without supporting clinical studies or bridging studies to a device which was the subject of the clinical studies. An hsCRP assay will need to submit a premarket notification and follow the guidance in order to expand their indications for use statement to include ***for use as an aid in the identification and stratification (assessment) of individuals at risk for future cardiovascular disease. When used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, cCRP may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndrome***

The designation "cCRP" is intended solely to identify IVDs which meet the performance specifications as described above, and use of this name is not a requirement imposed on laboratories performing this test. Since the name "hsCRP" has been in use when the test is used for cardiovascular risk assessment/stratification, FDA understands that laboratories may choose to continue to use this name. However, if such testing is performed using a non-cCRP kit, such use would constitute an off-label, or unapproved, use of the device. While physicians may order and use tests based on their experience and knowledge, regardless of FDA approval, the manufacturer may not promote or

encourage such off label use. Further, under the provisions of CLIA, the laboratory must validate the test performance if it performs the test in a manner not consistent with the manufacturer's recommendations and intended use.